

REMARKS

On August 23, 2002, the Patent Office mailed a Notice of Withdrawal from Issue Under 37 CFR 1.313(b). A subsequent communication from the Office was mailed on October 1, 2002, indicating that prosecution of the instant application was being suspended. In that October 1, 2002 Office Action, the Examiner confirmed that claims 9 and 10 had been canceled without prejudice by way of Examiner's Amendment.

As an initial point, Applicant wishes to clarify that the Examiner had been granted the authority to cancel claim 8, in addition to claims 9 and 10, without prejudice. To avoid any confusion in the record, claim 8 is being canceled by the amendment herein. Claim 29 has also been amended so as not to depend from now canceled claims 8 and 10.

In view of the cancellation of claims 8 to 10, a request to amend inventorship under 37 CFR 1.48(b) is enclosed herewith. Applicant respectfully requests that the inventorship for the instant application be amended to reflect Avi J. Ashkenazi as the sole named inventor.

Claims 21-41 remain pending in this application. For the Examiner's convenience, a clean copy of all pending claims is provided above. In the attached page entitled "Marked Up Version to Show Changes Made", the amendments to claims 8 and 29 are shown.

Each of the rejections set forth in the instant Office Action are addressed below.

Section 112 Rejection

Claim 28 was rejected under Section 112, first paragraph, as being directed to subject matter that the Examiner believes was not sufficiently described in the application to demonstrate that the

applicant was in possession of the claimed invention at the time the application was filed. Applicant respectfully traverses this rejection.

The Examiner's attention is respectfully directed to page 9, lines 22-23, wherein there is provided a description of "dimeric molecules, in particular homodimeric molecules, comprising Apo-2 antibody." The Examiner's attention is further directed, for example, to page 52, lines 35-42, wherein homodimeric molecules comprising anti-Apo-2 antibody are described.

It is submitted that the terms "dimer" or "dimeric" are terms of art readily understood by those skilled in the art to mean "two" or a molecule having "two" components. In view of the present application, this is particularly understood as the disclosure teaches various antibody constructs which include more than one antibody molecule, including where two antibody molecules that are joined are the same antibody (i.e., a "homodimeric" molecule).

In view of the above, Applicant respectfully requests withdrawal of the rejection of claim 28 under 35 U.S.C. 112, first paragraph.

Rejection Under Section 102(e)

In the instant Action, claims 21-27 and 34-41 have been rejected under Section 102(e) as being anticipated by US Patent 6,072,047 ("the '047 patent"). Applicant requests withdrawal of this rejection on the basis of the following remarks.

As a preliminary point, Applicant notes that the '047 patent was previously considered by the Examiner during prosecution of the instant application. Applicant notes in particular the copy of the Form 1449 provided with the Office communication of October 1, 2002, which was signed by the Examiner on May 1, 2002. This document indicates that the contents of the '047 patent relative to the

rejected claims were fully considered prior to the issuance of the notice of allowance by the Office. The Examiner concluded after a full consideration of the contents of the '047 patent that the above-cited claims were patentable.

Also, before addressing the substance of the rejection, Applicant wishes to correct a factual error made by the Office at page 3, lines 4 to 6 of the Office Action. Applicant notes that the length of the amino acid insert being addressed is 29 amino acids, not 39 amino acids, as is stated in the Office action.

To anticipate a claim under section 102(e), the disclosure of the cited patent reference must describe each limitation of the claimed invention. See, In re Robertson, 169 F.3d 743, 745 (Fed. Cir. 1999). Where that patent claims the benefit of one or more earlier filed applications to which the patent has made a claim under 35 U.S.C. 120, the contents of each such earlier filed application must be considered relative to the claimed invention. See, M.P.E.P. 2136.03(IV). If one or more of the earlier filed applications do not contain the same disclosure as the patent, the patent may not be entitled to the priority date of the earlier filed applications. A patent is entitled to a prior art effective date under 102(e) in relation to an earlier filed application to which a claim under 35 U.S.C. 120 is made only if the disclosure of the earlier filed application supports the claims under 35 U.S.C. 112. See, e.g., In re Wertheim, 646 F.2d 527, 537 (C.C.P.A. 1981). The '047 patent fails to meet these requirements.

The '047 patent issued from patent application serial no. 08/883,036 filed June 26, 1997, which in turn claims priority to a series of continuation-in-part application filings on February 13, 1997; March 12, 1997; March 28, 1997; and June 4, 1997, respectively.¹ A review of each of those four priority applications demonstrates that none filed prior to the May 15, 1997 priority date of the instant

¹ Copies of each of these four respective priority applications are attached as Exhibits C-F to the Rule 131 Declaration being filed concurrently with this Amendment and Response.

application contain any disclosure directed to the claimed subject matter in the instant application.

A review of each of these applications reveals that there is no disclosure of an antibody having the characteristics recited in the rejected claims in any of the '047 patent priority applications filed prior to the instant application's priority date (i.e., May 15, 1997). In particular, there is no disclosure in any of the applications filed prior to May 15, 1997, prophetic or otherwise, of an Apo-2 receptor (or "TRAIL-R") specific antibody that has apoptosis-inducing activity, or of a use of such antibody. The '047 patent priority applications filed on February 13, March 12, and March 28, 1997 are all silent with respect to such agonistic or apoptosis-inducing antibodies.

Applicant further notes that the Examiner has cited various portions of the '047 patent disclosing generic teachings of means of producing antibodies. In contrast, the claims in the instant application recite specific attributes of Apo-2 receptor antibodies, particularly certain functional properties recited in the claims. These general teachings of the '047 patent do not describe an antibody that has the characteristics of the claimed antibodies, and as such, cannot anticipate the claims.

The Examiner also refers at page 3, lines 10-11 of the Office Action to a provision in the '047 patent concerning "agonist antibodies that mimic ligand binding are described as inducing apoptosis of certain cancer cells (col. 21, lines 35-46)". The Examiner seems to imply that this provision in the '047 patent is entitled to an effective filing date of March 28, 1997. Applicant respectfully submits that this is not the case, and in fact the '047 patent priority documents demonstrate that the referenced disclosure to "agonist antibodies" was not added until the June 4, 1997 filing -- after the effective filing date of the present application. The Examiner, in particular, is invited to compare pages 18 to 20 of the application 08/829,536 (filed March 28, 1997) to page 27, lines 3 to

10 of application 08/869,852 (filed June 4, 1997). The latter application, for the first time, added the following paragraph:

"Antibodies raised against TRAIL-R may be screened for agonistic (i.e., ligand-mimicking) properties. Such antibodies, upon binding to cell surface TRAIL-R, induce biological effects (e.g., transduction of biological signals) similar to the biological effects induced when TRAIL binds to cell surface TRAIL-R. Agonistic antibodies may be used to induce apoptosis of certain cancer cells or virally infected cells, as has been reported for TRAIL. The ability of TRAIL to kill cancer cells (including but not limited to leukemia, lymphoma, and melanoma cells) and virally infected cells is described in Wiley et al. (Immunity 3:673-682, 1995); and in PCT application WO 97/01633."

This demonstrates that no application to which the '047 patent claims priority contains any disclosure of an antibody having the properties or characteristics recited in the rejected claims prior to the effective filing date of the present application.

Applicant further notes that there is no disclosure in either the '047 patent or in any of the applications to which it claims priority of any hybridomas or antibodies that were actually produced, much less an antibody with the functional characteristics recited in the pending claims.

Because none of the '047 patent priority applications filed prior to the effective filing date of the present application disclose any of the elements of the claimed antibodies, the '047 patent does not anticipate the present claims.

Finally, Applicant provides herewith a Declaration under 37 CFR 1.131 executed by the inventor of the present application, Dr. Avi Ashkenazi. The Declaration establishes that none of the '047 patent

priority applications filed prior to the priority date of the instant application contain any disclosure of an antibody having the characteristics recited in the pending claims. The Declaration further establishes that the priority date of the present application antedates the filing date of the '047 patent with respect to the claimed antibodies.

Section 103 Rejection

Claims 30-33 were rejected under Section 103(a) as being unpatentable over US Patent 6,072,047 (the '047 patent), in view of US Patent 6,455,262 (the '262 patent), Ghetie et al., and Shopes. Applicant respectfully traverses this rejection.

As an initial point, the '047 patent contains no disclosure prior to the effective filing date of the present application of an antibody having the characteristics of the claimed antibodies. As such, the '047 patent does not teach "[a]gonist antibodies that mimic ligand binding ... as inducing apoptosis of certain cancer cells..." as suggested at page 3 of the Office Action. The '047 patent is, thus, not prior art against the claimed invention under 102(e) as represented by the Office. Withdrawal of the Section 103 rejection is requested on this basis.

In addition, the remainder of the disclosure of the '047 patent cannot establish a prima facie basis for rejecting the pending claims under 35 U.S.C. 103. In particular, Applicant submits that the combined teachings of the '047 patent (based on the disclosures of the applications to which the '047 patent claim priority filed prior to the effective filing date of the present application), when taken in view of the disclosures of the '262 patent, Ghetie et al., and Shopes do not teach or suggest the claimed antibodies.

To establish a prima facie basis for obviousness under 35 U.S.C. 103, based on multiple prior art disclosures, the Office must be able to point to some teaching, suggestion or reason in the disclosures to

combine them to arrive at the claimed invention. Gambro Lundia v. Baxter Healthcare, 110 F.3d 1573 (Fed. Cir. 1997); Teleflex, Inc. v. Ficosa North American Corp., 299 F.3d 1313 (Fed. Cir. 2002). Moreover, a finding that a prior art reference teaches away from the claimed invention is enough to defeat a prima facie claim of obviousness. See, e.g., Winner International Royalty Corp. v. Wang, 202 F.3d 1340 (Fed. Cir. 2000).

The disclosures of the applications to which the '047 patent claims priority which were filed prior to May 15, 1997 actually teach away from the claimed antibodies. Those disclosures suggest that anti-TRAIL-R antibodies may be useful therapeutically as agents which block ligand activity or binding to TRAIL receptor, not as agonistic agents which induce apoptosis (i.e., ligand-mimicking activity). In other words, the teachings of those disclosures postulate a utility for anti-TRAIL-R antibodies requiring the antibodies to interfere with ligand activity or ligand-receptor binding, not to mimic such ligand-receptor binding. Examples of diseases cited in these priority applications suggest that the applicant postulated that diseases that could be treated by such antibodies are disorders associated with improper TRAIL (ligand) expression (see, e.g. p. 20, application no. 08/829,536 filed March 28, 1997) - not diseases that could be treated by an apoptosis-inducing (i.e., ligand-mimicking) antibody.

Thus, the '047 patent priority disclosures filed prior to the effective filing date of the present application do not provide any motivation, suggestion or guidance to one skilled in the art to make or identify agonistic antibodies that mimic the apoptosis-inducing activity of the ligand.

For at least these reasons, there would be no motivation to the skilled artisan to combine the teachings of the Ghetie et al. or Shopes with the '047 patent to achieve apoptosis-inducing antibodies to the Apo-2 receptor.

An obviousness rejection also cannot be predicated on the mere identification of individual features or attributes of a claimed invention in the prior art references. Rather, particular findings must be made as to the reason why one of ordinary skill in the art, without the benefit of hindsight, would have selected the components for combination as was done in the claimed invention. See, e.g., In re Kotzab, 217 F.3d 1365 (Fed. Cir. 2000). Therefore, as any teachings of human, homodimeric or dimeric antibodies in the '262 patent, Ghetie et al. or Shopes, are not directed to antibodies specific for the Apo-2 receptor, an ordinarily skilled artisan would not have been motivated to combine the teachings of those references with the '047 patent to arrive at the claimed invention. As such, those references do not fill the gaps left by the '047 patent.

For these reasons, it is respectfully submitted that the Office has not met its burden in presenting a prima facie basis of obviousness of the presented claims and the Applicant respectfully requests that the Office withdraw this rejection of the presented claims.

Applicant submits that the above remarks and the enclosed Rule 131 Declaration clearly establish that the '047 patent does not anticipate the presented claims, and does not have an effective filing date under 35 U.S.C. § 102(e) prior to the effective filing date of the present application with respect to the claims pending in the instant application. The combined teachings of the four references cited by the Examiner likewise do not render the claims obvious under Section 103(a). Withdrawal of these rejections is hereby requested.

In view of this submission, along with the Examiner's consideration of the relevant art and already completed review of the instant application for compliance with 35 U.S.C. 101 and 112, Applicant believes there is no basis for the Office to withhold


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issuance of this application. Applicant respectfully requests the Office to issue the present application.

If the Examiner believes that the present submission does not fully address the rejection presented in the Office Action, the undersigned respectfully requests an interview to discuss these issues.

Respectfully submitted,
GENENTECH, INC.

Date: October 21, 2002

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MARKED UP VERSION TO SHOW CHANGES MADE

In the claims:

Please cancel claim 8 without prejudice.

29. (Amended) A homodimeric molecule comprising any two antibodies of claims [8, 10,] 21, 22, 23 or 24.